

THE ROCKEFELLER UNIVERSITY

NEW YORK, N.Y. 10021

May 9, 1973

Dr. Frederic W. Nordsiek
The Council for Tobacco Research - U.S.A., Inc.
110 East 59th Street
New York, N. Y. 10022

Dear Dr. Nordsiek:

At Dr. Neal Miller's suggestion, I have reviewed Dr. Thomas C. Westfall's proposal to the Council for Tobacco Research entitled "Action of Nicotine on Peripheral and Central Neurons in Animals Chronically Exposed to Nicotine."

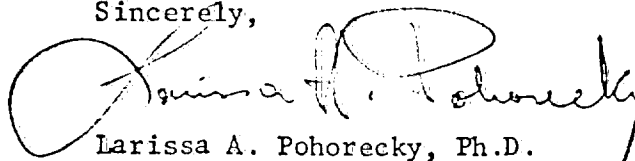
In my opinion, the proposal is well organized and well written. Dr. Westfall has sufficient knowledge and previous experience in the catecholamine field and in nicotine research to be able to conduct these experiments effectively. The results from the proposed experiments will contribute significantly to the knowledge on the chronic effects of nicotine in rodents.

The grant proposal provides good background information on the proposed experiments and on the literature in the field. Dr. Westfall's working hypothesis is scientifically sound and the experimental design is well directed toward the specific aims of the project. The length of time for the project, and the budget requested, appear to me quite adequate.

As far as the experimental design is concerned, I would suggest only two points. First, that it would be useful to include the determination of both monoamine oxidase and catechol-O-methyl transferase activities not only on liver and heart as described by Dr. Westfall, but also on the brain samples. It is very likely that, if the activities of these two norepinephrine-catabolyzing enzymes are altered by nicotine in peripheral organs (liver and heart) as stated in the proposal, a change in the activities of both enzymes might also occur in central noradrenergic neurons. This, in fact, might be quite significant in the adjustment of the central noradrenergic neurons to chronic nicotine exposure.

Secondly, in the experiments where the release of labeled amines will be examined in chopped brain slices, I think that it is very important to first examine whether there are any differences in the uptake of the labeled monoamines by the tissues obtained from animals exposed to nicotine chronically. Thus, the subsequently examined release of the labeled amines might be confounded by an unequal pre-labeling of the brain slices.

Sincerely,


Larissa A. Pohorecky, Ph.D.

LAP:emg

1003542183